WO 91/04058 PCT/CA90/00306

70

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE AS FOLLOWS:

- A combination for administration to a mammal which combination employs a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition and an amount of hyaluronic acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
- 2. The combination of Claim 1 wherein the hyaluronic 15 acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is an amount of hyaluronic acid and/or salts.
- 3. The combination of Claim 1 or 2 wherein the medicinal and/or therapeutic agent comprises an agent selected from a free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungal agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia anti-body monoclonal agent, minoxidil for topical application for hair growth, diuretics, immunosuppressants, lymphokynes, alpha-and-B-interferon and combinations thereof.

30

35

- 4. The combination of Claim 2 wherein the medicinal and/or therapeutic agent comprises an agent selected from ascorbic acid, an anti-cancer agent, non-steroidal anti-inflammatory drugs, antibiotics, diuretics and combinations thereof.
- 5. The combination of Claim 1, 2 or 4 inclusive wherein the hyaluronic acid and/or salts thereof and or the

35

homologues, analogues, derivatives, complexes, esters, fragments and subunits are separate from the medicinal and/or therapeutic agent.

- 5 6. The combination of Claim 1, 2 or 4 wherein the combination is to be administered concurrently.
 - 7. The combination of Claim 1, 2 or 4 wherein the combination is to be administered at the identical site.
- 8. A formulation suitable for use to treat a condition or disease, the formulation comprising a therapeutically effective amount of a medicinal and/or therapeutic agent to treat the disease or condition in an amount of hyaluronic acid and/or salts thereof sufficient to facilitate the penetration of the agent at site to be treated through the tissue (including scar tissue) through cell membranes into the individual cells to be treated.
- 20 9. The formulation of Claim 8 wherein the medicinal and/or therapeutic agent comprises an agent selected from free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia, anti-body monoclonal agent, minoxidil for topical application for hair growth, diuretics, immunosuppressants, lymphokynes, alpha-and-30 ß-interferon and combinations thereof.
 - 10. The formulation of Claim 8 or 9 wherein the medicinal and/or therapeutic agent is selected from ascorbic acid, an anti-cancer agent, non-steroidal anti-inflammatory drugs, antibiotics, diuretics and combinations thereof.
 - 11. A method of treating a condition or disease in a mammal comprising administering to the mammal a

therapeutically effective amount of a medicinal and/or therapeutic agent to treat the disease or condition and a sufficient amount of hyaluronic acid and/or salts and/or homologues, analogues, derivatives, complexes, esters, fragments, and sub-units of hyaluronic acid thereof sufficient to facilitate the penetration of the agent through the tissue (including scar tissue) at the site to be treated through the cell membranes into the individual cells to be treated.

- 10 12. The method of treating a condition or disease in a mammal of Claim 11, wherein the hyaluronic acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is an amount of hyaluronic acid and/or salts thereof.
- 15 13. The method of Claim 11 or 12 wherein the medicinal and/or therapeutic agent is selected from a free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-20 inflammatory drugs (NSAID), steroidal anti-inflammatory drugs anti-fungal agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia, anti-body monoclonal agent, minoxidil for topical application for hair growth, 25 diuretics, immunosuppressants, lymphokynes, alpha-and-ßinterferon and combinations thereof.
- 14. The method of Claim 11, 12 or 13 wherein the medicinal and/or therapeutic agent is selected from ascorbic acid, an anti-cancer agent, non-steroidal anti-inflammatory drugs, antibiotics, diuretics and combinations thereof.
- 15. The method of Claim 11, 12, 13 or 14 wherein the combination is administered simultaneously at the identical site.
 - 16. A method of treating disease or condition in a mammal, comprising administering to the mammal a

therapeutically effective amount of a formulation comprising a therapeutically effective amount of a medicinal and/or therapeutic agent to treat the disease or condition carried in an amount of hyaluronic acid and/or salts thereof sufficient to facilitate the penetration of the agent at the site to be treated through the tissue (including scar tissue) through cell membranes into the individual cells to be treated.

The method of Claim 16 wherein the medicinal and/or 10 therapeutic agent is selected from a free radical scavenger, acid, Vitamin C, an anti-cancer chemotherapeutic agent, anti-viral agents, non-steroidal antiinflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungal agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for 15 the treatment of vascular ischemia anti-body, monoclonal agent, minoxidil for topical application for hair growth, diuretics, immunosuppressants, lymphokynes, alpha-and-ßinterferon and combinations thereof.

18. The method of Claim 16 or 17 wherein the medicinal and/or therapeutic agent is selected from ascorbic acid, an anti-cancer agent, non-steroidal anti-inflammatory drugs, antibiotics, diuretics and combinations thereof.

25

20

19. For delivery of a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition in a mammal, a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the penetration of the agent at the site to be treated through the cell membranes into the individual cells to be treated.

35

30

20. For delivery of a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition in a mammal, a sufficient amount of hyaluronic acid

25

and salts thereof to facilitate the penetration of the agent at the site to be treated through the cell membranes into the individual cells to be treated.

- 5 21. For delivery according to Claim 19 or 20 wherein the medicinal and/or therapeutic agent is selected from a free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia, anti-body monoclonal agent, minoxidil for topical application for hair growth, diuretics, immunosuppressants, lymphokynes, alpha-and-B-interferon and combinations thereof.
 - 22. For delivery according to Claim 21 wherein the medicinal and/or therapeutic agent is selected from ascorbic acid, an anti-cancer agent, non-steroidal anti-inflammatory drugs, antibiotics, diuretics and combinations thereof
 - 23. The combination of Claim 2, 3 or 4 wherein the hyaluronic acid and/or salts thereof utilized at a dose of from about 10 to 1000 mg/70 kg person.
 - 24. The formulation of Claim 8, 9 or 10 inclusive wherein the hyaluronic acid and/or salts thereof is utilized at a dose of from about 10 to 1000 mg/70 kg person.
- 30 25. The method of Claim 11, 12, 13, 14, 15, 16, 17 or 18 inclusive wherein the hyaluronic acid and/or salts thereof is utilized at a dose of from about 10 to 1000 mg/70 kg person.
- 26. The combination for the treatment of psoriasis of a therapeutically effective amount of methotrexate with hyaluronic acid and/or salts thereof sufficient to facilitate the methotrexate's penetration through the tissue of the site to be treated.

- 27. The combination of Hyaluronic acid and/or salts thereof with a cytotoxic chemotherapeutic agent selected from adriamycin, methotrexate, mitomycin C, bleomycin, 5-5 Fluorouracil, novantrone, carbo and cis platinum, and combinations thereof.
- 28. The combination of an agent selected from phloridzin, phloretin, and 5-deoxyglucuronide of phloridzin;

 10 Vitamin C; and a non-steroidal anti-inflammatory drug, and combinations thereof to competitively block glucose transport in neoplastic cells and an amount of hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated and where phloretin is the selected agent, it is solubilized by a solubilizing such as N methyl glucamine.
- 29. The combination of a therapeutically effective amount of a brohchodilator with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

30

- 30. The combination of a therapeutically effective amount of alpha 2 interferon with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
- 31. The combination of a therapeutically effective amount of a diuretic with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

- 32. The combination of a therapeutically effective amount of a medicinal and/or therapeutic agent selected from an antibiotic and/or anti-bacterial agent with hyaluronic acid an/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
- 10 33. The combination of a therapeutically effective amount of ascorbic acid (Vitamin C) for the treatment of mononucleosis with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
 - 34. The combination of a therapeutically effective amount of minoxidil for the growing of hair on a mammal with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
- 25 35. The combination of a therapeutically effective amount of a non-steroidal anti-inflammatory drug (NSAID) with hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
 - 36. The combination of a therapeutically effective amount of an immunosuppressant and hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

WO 91/04058 PCT/CA90/00306

77

37. The combination of a therapeutically effective amount of an anti-viral agent and hyaluronic acid and/or salts thereof.

- 5 38. The combination of Claim 37 where the antiviral agent is a nonionic surfactant.
 - 39. The combination of Claim 38 wherein the anti-viral agent is nonoxynol-9.

10

15

40. A combination or formulation suitable for use to treat a condition or disease, the formulation comprising a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition in an amount of hyaluronic acid and/or salts thereof and dimethyl sulfoxide sufficient to transport the agent to the site to be treated and to penetrate through the tissue (including scar tissue) through cell membranes into the individual cells to be treated.

20

41. The combination or formulation of Claim 40 wherein the agent comprises a compound selected from phloridzin, phloretin and 5-deoxyglucuronide of phloridzin, ascorbic acid and a non-steroidal anti-inflammatory drug.

25

- 42. The combination or formulation of Claim 2 wherein the agent comprises a compound selected from phloridzin, phloretin and 5-deoxyglucuronide of phloridzin.
- 30 43. For the treatment of diabetes, the combination of a therapeutically effective amount of insulin and hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
 - 44. For the treatment of post-menopausal female mammals, the combination of a therapeutically effective amount of

estrogen and hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

5

10

25

- 45. For the control of fertility, the combination of a therapeutically effective amount of progestegen and hyaluronic acid and/or salts thereof sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.
- 46. For use to treat a disease or condition in a mammal with a medicinal and/or therapeutic agent, a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at a site in the mammal to be treated by the agent passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
 - 47. For use to treat a disease or condition in a mammal a therapeutically effective amount of a medicinal and/or therapeutic agent with a sufficient amount of hyaluronic acid and salts thereof to facilitate the agent at a site in a mammal to be treated by the agent passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 30 48. For the use according to Claim 46 or 47 wherein the agent is selected from a free radical scavenger, ascorbic acid, Vitamin C, an anti-cancer agent, chemotherapeutic agent, anti-viral agents, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungi agent, detoxifying agents, analgesic, bronchodilator, anti-bacterial agent, antibiotics, drugs for the treatment of vascular ischemia, anti-body monoclonal agent, minoxidil for topical application for hair growth, diuretics, immunosuppressants,

30

lymphokynes, alpha-and-B-interferon and combinations thereof.

- 49. The use of Claim 46, 47 or 48 wherein the hyaluronic acid and/or salts thereof is utilized at a dose of from about 10 to 1000 mg/70 kg person.
 - 50. The combination of Claim 1 or 2 wherein the agent is an anti-cancer agent.
- 10 51. The combination of Claim 1 or 2 wherein the agent is an anti-viral agent.
 - 52. The combination of Claim 1 or 2 wherein the agent is an anti-fungal agent.
- 53. The combination of Claim 1 or 2 wherein the agent is an analgesic.
- 54. The combination of Claim 1 or 2 wherein the agent is 20 a bronchodilator.
 - 55. The combination of Claim 1 or 2 wherein the agent is an anti-bacterial agent.
- 25 56. The combination of Claim 1 or 2 wherein the agent is an antibiotic.
 - 57. The combination of Claim 1 or 2 wherein the agent is and anti-inflammatory agent.
 - 58. The combination of Claim 1 or 2 wherein the agent is an anti-body monoclonal agent.
- 59. The combination of Claim 1 or 2 wherein the agent is an immunosuppressant.
 - 60. The combination of Claim 1 or 2 wherein the agent is a lymphokynes.

- 61. The combination of Claim 60 wherein the lymphokyne is interleukin 2.
- 5 62. The combination of Claim 1 or 2 wherein the agent is interferon.
 - 63. The formulation of Claim 8 wherein the agent is an anti-cancer agent.

- 64. The formulation of Claim 8 wherein the agent is and anti-viral agent.
- 65. The formulation of Claim 8 wherein the agent is an analgesic.
 - 66. The formulation of Claim 8 wherein the agent is a bronchodilator.
- 20 67. The formulation of Claim 8 wherein the agent is an anti-bacterial agent.
 - 68. The formulation of Claim 8 wherein the agent is an antibiotic.

25

- 69. The formulation of Claim 8 wherein the agent is an anti-inflammatory agent.
- 70. The formulation of Claim 8 wherein the agent is and 30 anti-body monoclonal agent.
 - 71. The formulation of Claim 8 wherein the agent is an immunosuppressant.
- 35 72. The formulation of Claim 8 wherein the agent is a lymphokyne.
 - 73. The formulation of Claim 72 wherein the lymphokyne SUBSTITUTE SHEET

is interleukin - 2.

74. The formulation of Claim 8 wherein the agent is interferon.

5

- 75. The combination of claim 1 or 2 wherein the agent is ascorbic acid (Vitamin C).
- 76. The combination of claim 1 or 2 wherein the agent is 10 a free radical scavenger.
 - 77. The combination of claim 1 or 2 wherein the agent is a chemotherapeutic agent.
- 15 78. The combination of claim 1 or 2 wherein the agent is a non-ionic surfactant.
 - 79. The combination of claim 1 or 2 wherein the agent is a non-steroidal anti-inflammatory drugs (NSAID).

20

- 80. The combination of claim 1 or 2 wherein the agent is a steroidal anti-inflammatory drug.
- 81. The combination of claim 1 or 2 wherein the agent is 25 a detoxifying agent.
 - 82. The combination of claim 1 or 2 wherein the agent is a drug for treating vascular ischemia.
- 30 83. The combination of claim 1 or 2 wherein the agent is minoxidil for topical application for hair growth.
 - 84. The combination of claim 1 or 2 wherein the agent is a diuretic.

35

85. The combination of claim 78 wherein the non-ionic surfactant is nonoxynol-9.

86. The combination of claim 78 wherein the non-ionic surfactant comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule.

- 5 87. The combination of claim 79 wherein the non-steroidal anti-inflammatory drug is selected from indomethacin, naproxen and the (+/-) tromethamine salt of ketorolac and combinations thereof.
- 10 88. The combination of claim 84 wherein the diuretic is furosemide.
 - 89. The formulation of claim 8 wherein the agent is ascorbic acid.

15

- 90. The formulation of claim 8 wherein the agent is a free radical scavenger.
- 91. The formulation of claim 8 wherein the agent is a 20 chemotherapeutic agent.
 - 92. The formulation of claim 8 wherein the agent is a non-ionic surfactant.
- 25 93. The formulation of claim 8 wherein the agent is a non-steroidal anti-inflammatory drug (NSAID).
 - 94. The formulation of claim 8 wherein the agent is a steroidal anti-inflammatory drug.

30

- 95. The formulation of claim 8 wherein the agent is a detoxifying agent.
- 96. The formulation of claim 8 wherein the agent is a drug for treating vascular ischemia.
 - 97. The formulation of claim 8 wherein the agent is minoxidil for topical application for hair growth.

35

- 98. The formulation of claim 8 wherein the agent is a diuretic.
- 5 99. The formulation of claim 92 wherein the non-ionic surfactant is nonoxynol-9.
- 100. The formulation of claim 92 wherein the non-ionic surfactant comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule.
 - 101. The formulation of claim 93 wherein the non-steroidal anti-inflammatory drug is selected from indomethacin, naproxen and the (+/-) tromethamine salt of ketorolac and combinations thereof.
 - 102. The formulation of claim 98 wherein the diuretic is furosemide.
- 20 103. A combination suitable for use to treat a person with AIDS, the combination comprising therapeutically effective amounts of ascorbic acid (Vitamin C), non-steroidal anti-inflammatory drugs, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues,
- 25 derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at a site to be treated through the tissue (including scar tissue) through cell membranes into the individual cells to be treated.
- 30 104. The combination of claim 103 wherein the amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is hyaluronic acid and/or salts thereof.

105. The combination of claim 103 or 104 further comprising interferon.

- 106. The combination of claim 103 or 104 wherein the non-steroidal anti-inflammatory drug is indomethacin.
- 107. The combination of claim 103, 104, 105 or 106 wherein the amount of hyaluronic acid and salts thereof or other forms thereof may be substituted by dimethyl sulfoxide (either in whole or in part).
- 108. A combination suitable for use to treat a person with cancer, the combination comprising therapeutically effective amounts of ascorbic acid (Vitamin C), non-steroidal anti-inflammatory drugs, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at a site to be treated through the tissue (including scar tissue) through cell membranes into the individual cells to be treated.
- 109. The combination of claim 108 wherein the amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 25 110. The combination of claim 108 or 109 wherein the non-steroidal anti-inflammatory drug is selected from indomethacin, naproxen and the (+/-) tromethamine salt of ketorolac.
- 30 111. For the treatment of cancer, the administration of a therapeutically effective amount of ascorbic acid, a non-steroidal anti-inflammatory drug, and at least one of an agent selected from an anti-cancer drug chemotherapeutic agent and detoxifying drug, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue)

through the cell membranes into the individual cells to be treated.

- 112. For the use of claim 111 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 113. For the use of claim 111 or 112 wherein the non10 steroidal anti-inflammatory drug is selected from indomethacin, naproxen and ketorolac trimethamine.
- 114. For hair growth, the topical administration of a therapeutically effective amount of minoxidil and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 115. For use to treat herpes, canker sores and shingles, the administration of a therapeutically effective amount of nonionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 116. For the use of Claim 115 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 117. For the use of Claim 115 or 116 wherein the nonionic

surfactant comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule.

- 118. For the use in Claim 115 or 116, the nonionic surfactant is nonoxynol-9.
- 119. treat renal failure, For use to insufficiency, hypertension and edema, the administration of an effective amount of a diuretic and a sufficient amount of 10 hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the 15 individual cells to be treated.
 - 120. For the use of Claim 119 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 121. For the use of Claim 119 and 120 wherein the diuretic is furosemide.
- 25 122. For use to treat infection, the administration of a therapeutically effective amount of an agent selected from antibiotics, antibacterials, antimicrobials and combinations therof with or without ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

35

20

123. For the use of Claim 122 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives,

complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

5 124. For use to treat acne, the administration of a therapeutically effective amount of an agent selected from antibiotics, antibacterials, antimicrobicals and combinations therof with or without ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

15

125. For the use of Claim 124 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

20

25

30

35

- 126. For use in the transplant of organs and tissue to reduce the likelihood of the rejection thereof, the administration of a therapeutically effective amount of an immunosuppressant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 127. For the use in Claim 126 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 128. For the use in Cliam 126 or 127 wherein the

immunosuppressant is a cyclosporin.

- 129. For use in treating inflammation, the administration of a therapeutically effective amount of a non-steroidal antiinflammatory agent (NSAID) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue
 (including scar tissue) through the cell membranes into the individual cells to be treated.
- 130. For the use in Claim 129 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 20 131. For use in assisting in the elimination of tumour break down material (including toxins, residue and debris) in a person suffering from tumours, the administration of a therapeutically effective amount of a non-steroidal anti-inflammatory agent (NSAID) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
 - 132. For the use in Claim 131 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 133. For the use of Claim 129, 130, 131 or 132 wherein

the non-steroidal anti-inflammatory agent (NSAID) is selected from indomethacin, naproxen and $[\pm]$ tromethamine salt of Ketorolac.

- 5 134. For use in detoxifying a patient of toxins, the administration of a therapeutically amount of a detoxifying agent and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 15 135. For the use of Claim 134 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 20 136. For the use of Claim 134 or 135 in the form of peritoneal dialysis.
- 137. For use to treat a patient suffering from respiratory difficulties, the administration of a 25 therapeutically effective amount of a bonchodilator or the like and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
 - 138. For the use of Claim 137 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 139. For use to treat vascular ischemia, the

administration of a therapeutically effective amount of an agent suitable for use to treat the condition and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 10 140. For the use of Claim 139 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 141. For use to treat a person suffering from AIDS (HIV virus) the administration of therapeutically effective amounts of, ascorbic acid (Vitamin C), a non-steroidal anti-inflammatory agent and an agent selected from interferon, an anti-viral agent, an antibiotic, dimethyl sulfoxide [DMSO] and combinations thereof; a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 142. For the use of Claim 141 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 143. For the use of Claim 141 or 142 wherein Dimethyl Sulfoxide (DMSO) is substituted for some or all of the forms of hyaluronic acid.
 - 144. For the use of Claim 141, 142 or 143 wherein the non-steriodal anti-inflammatory drug is selected from

indomethacin, naproxen and $[\pm]$ tromethamine salt of Ketorolac.

145. For use to treat herpes, the administration of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

146. For use to treat canker sores, the administration of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

20

25

10

15

147. For use to treat herpes zoster (shingles), the administration of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

30

35

148. For the use of Claim 145, 146 or 147 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is hyaluronic acid and/or salts thereof.

149. For the use of Claim 145, 146, 147 or 148, wherein the non-ionic sufactant comprises an ether or an amide linkage

between the hydrophilic and hydropholic portions of the molecule.

- 150. For the use of Claim 149 wherein the non-ionic surfactant comprises nonoxynol-9.
- 151. For use to treat infections surrounding implants in a patient, the administration of a therapeutically effective amount of an antibiotic for the infected tissue surrounding the implant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- tumours and in respect of which swelling has occurred, the administration of a therapeutically effective amount of dimethyl sulfoxide and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 30 153. The use of Claim 151 or 152 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 35 154. For the treatment of mononucleosis, the administration of a therapeutically effective amount of ascorbic acid (Vitamin C) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues,

10

15

20

25

analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 155. For the treatment of herpes simplex type I and II, the administration of a therapeutically effective amount of a non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 156. For the use of Claim 155 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 157. For the use of Claim 155 or 156 wherein the non-ionic surfactant comprises an ether or an amide linkage between the hydrophilic and hydropholic protions of the molecure.
- 158. For the use of Claim 157 wherein the non-ionic surfactant is nonoxynol-9.
- 30 159. For the use to treat herpes, herpes simplex type I and II and herpes zoster (shingles), the administration of a therapeutically effective amount of a surfactant selected from an anionic surfactant and a cationic surfactant and combinations thereof and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including

scar tissue) through the cell membranes into the individual cells to be treated.

- 160. For the use of Claim 159 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 161. For the use of Claim 159 or 160 wherein the anionic surfactant comprises cetyl pyridinium chloride and the like and the cationic surfactant comprises benzalkonium chloride and the like.
- 162. For the treatment of a patient suffering from cancer, the administration of a therapeutically effective amount of a non-steroidal anti-inflammatory agent a therapeutically effective amount of an anti-cancer agent, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes
- 25 163. For the use of Claim 162 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

into the individual cells to be treated.

- 30 164. For the use of Claim 162 or 163 further comprising a therapeutically effective amount of Ascorbic Acid (Vitamin C).
- 165. For the use of Claim 162, 163 or 164 wherein the non-steroidal anti-inflammatory agent is selected from indomethacin, naproxen and [±] tromethamine salt of Ketorolac.
 - 166. For use to treat canker sores, the administration of a therapeutically effective amount of (alpha) 2-interferon

with an amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid sufficient to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 167. For the use of Claim 166 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 168. For use to treat pain, the administration of a therapeutically effective amount of a non-steroidal anti15 inflammatory agent and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue)
 20 through the cell membranes into the individual cells to be treated.
- 169. For the use of Claim 168 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 170. For the use of Claim 168 or 169 wherein the nonsteriodal anti-inflammatory comprises indomethacin, naproxen 30 and a combination thereof.
 - 171. For the use of Claim 168 or 169 wherein the non-steroidal anti-inflammatory comprises $[\pm]$ tromethamine salt of Ketorolac.

172. For use to treat a patient suffering from HIV (AIDS), the administration of a therapeutically effective amount of Ascorbic Acid (Vitamin C), a therapeutically

effective amount of a non-steroidal anti-inflammatory and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 173. For the use of Claim 172 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 174. For the use of Claim 172 or 173 wherein the non-15 steroidal anti-inflammatory is indomethacin.
 - 175. For the use of Claim 154 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 176. For the treatment of cancer, the combination of a therapeutically effective amount of ascorbic acid, a non-steroidal anti-inflammatory drug, and at least one of an agent selected from an anti-cancer drug, chemotherapeutic agent and detoxifying drug, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 177. The combination of claim 176 wherein the hyaluronic 35 acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

-2

178. The combination of claim 176 or 177 wherein the non-steroidal anti-inflammatory drug is selected from indomethacin, naproxen and ketorolac tromethamine.

179. For hair growth, the combination 5 therapeutically effective amount of minoxidil, and at least agent selected from an anti-cancer one of an chemotherapeutic agent and detoxifying drug, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-10 units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

15

20

180. For use to treat herpes, canker sores and shingles, the combination of a therapeutically effective amount of nonionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

25

181. The combination of Claim 180 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

30

35

182. The combination of Claim 180 or 181 wherein the nonionic surfactant comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule.

183. For the use in Claim 180 or 181, the nonionic surfactant is nonoxynol-9.

- treat failure, 184: For use to renal cardiac insufficiency, hypertension and edema, the combination of an effective amount of a diuretic and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated. 10
 - 185. The combination of Claim 184 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 186. The combination of Claim 184 and 185 wherein the diuretic is furosemide.
- 20 187. For use to treat infection, the combination of a therapeutically effective amount of an agent selected from antibiotics, antibacterials, antimicrobials and combinations therof with or without ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

35

15

- 184. The combination of Claim 187 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 189. For use to treat acne, the combination of a

therapeutically effective amount of an agent selected from antibiotics, antibacterials, antimicrobicals and combinations therof with or without ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

. 10

190. The combination of Claim 189 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

15

20

25

- 191. For use in the transplant of organs and tissue to reduce the likelihood of the rejection thereof, the combination of an therapeutically effective amount of an immunosuppressant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 192. The combination of Claim 191 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, 30 derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
 - 193. The combination of Cliam 190 or 191 wherein the immunosuppressant is a cyclosporin.

35

194. For use in treating inflammation, the combination of a therapeutically effective amount of a non-steroidal anti-inflammatory agent (NSAID) and a sufficient amount of

hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 195. The combination Claim 194 wherein the hyaluronic 10 acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 196. For use in assisting in the elimination of tumour break down material (including toxins, residue and debris) in a person suffering from tumours, the combination of a therapeutically effective amount of a non-steroidal anti-inflammatory agent (NSAID) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
 - 197. The combination of Claim 132 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 198. The combination of Claim 194, 195, 196 or 197 wherein the non-steroidal anti-inflammatory agent (NSAID) is selected from indomethacin, naproxen and [±] tromethamine salt of Ketorolac.
 - 199. For use in detoxifying a patient of toxins, the

combination of a therapeutically amount of a detoxifying agent and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 10 200. The combination of Claim 199 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 201. The combination of Claim 199 or 200 in the form of peritoneal dialysis.
- 202. For use to treat a patient suffering from respiratory difficulties, the combination of a therapeutically effective amount of a bonchodilator or the like and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 203. The combination of Claim 202 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 204. For use to treat vascular ischemia, the combination of a therapeutically effective amount of an agent suitable for use to treat the condition and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site

PCT/CA90/00306

35

to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 5 205. The combination Claim 204 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- For use to treat a person suffering from AIDS (HIV 10 206. virus), the combination of therapeutically effective amounts of, ascorbic acid (Vitamin C), a non-steroidal antiinflammatory agent and an agent selected from interferon, an anti-viral agent, an antibiotic, dimethyl sulfoxide [DMSO] and and thereof a sufficient amount of hyaluronic 15 combinations acid and salts thereof and/or homologues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual 20 cells to be treated.
- 207. The combination of Claim 206 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 208. The combination of Claim 206 or 207 wherein Dimethyl Sulfoxide (DMSO) is substituted for some or all of the forms 30 of hyaluronic acid.
 - 209. The combination of Claim 206, 207 or 208 wherein the non-steriodal anti-inflammatory drug is selected from indomethacin, naproxen and $[\pm]$ tromethamine salt of Ketorolac.
 - 210. For use to treat herpes, the combination of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or

homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

211. For use to treat canker sores, the combination of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

15

10

5

212. For use to treat herpes zoster (shingles), the combination of a therapeutically effective amount of non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

25

30

35

- 213. The combination of Claim 210, 211 or 212 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 214. The combination of Claim 210, 211, 212 or 213, wherein the non-ionic sufactant comprises an ether or an amide linkage between the hydrophilic and hydropholic portions of the molecule.
- 215. The combination of Claim 214 wherein the non-ionic surfactant comprises nonoynol-9.

35

216. For use to treat infections surrounding implants in a patient, the combination of a therapeutically effective amount of an antibiotic for the infected tissue surrounding the implant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 217. For use to test a patient suffering from brain tumours and in respect of which swelling has occurred, the administration of a therapeutically effective amount of dimethyl sulfoxide and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 25 218. The combination of Claim 216 or 217 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid is hyaluronic acid and/or salts thereof.

219. For the treatment of mononucleosis, the combination of a therapeutically effective amount of ascorbic acid (Vitamin C) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be

30

35

treated.

- 220. For the treatment of herpes simplex type I and II, the combination of a therapeutically effective amount of a non-ionic surfactant and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 221. The combination of Claim 220 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 222. The combination of Claim 220 or 221 wherein the non-ionic surfactant comprises an ether or an amide linkage
 20 between the hydrophilic and hydropholic protions of the molecure.
 - 223. For the use of Claim 222 wherein the non-ionic surfactant is nonoxynol-9.
 - 224. For the use to treat herpes, herpes simplex type I and II and herpes zoster (shingles), the administration of a therapeutically effective amount of a surfactant selected from an anionic surfactant and a cationic surfactant and combinations thereof and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
 - 225. The combination of Claim 224 wherein the hyaluronic

WO 91/04058 PCT/CA90/00306

106

acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

- 5 226. The combination of Claim 223 or 224 wherein the anionic surfactant comprises cetyl pyridinium chloride and the like and the cationic surfactant comprises benzalkonium chloride and the like.
- 10 227. For the use of Claim 219 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 228. For the treatment of a patient suffering from cancer, the combination of a therapeutically effective amount of a non-steroidal anti-inflammatory agent a therapeutically effective amount of an anti-cancer agent, and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, 20 analogues, derivatives, complexes, esters, fragments and sub-
- analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

25

229. The combination of Claim 228 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

30

- 230. The combination of Claim 228 or 229 further comprising a therapeutically effective amount of Ascorbic Acid (Vitamin C).
- 35 231. The combination of Claim 228, 229 or 230 wherein the non-steroidal anti-inflammatory agent is selected from indomethacin, naproxen and [±] tromethamine salt of Ketorolac.

- 232. For use to treat canker sores, the combination of a therapeutically effective amount of alpha 2-interferon with a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid sufficient to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 10 233. The combination of Claim 232 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 234. For use to treat back pain, the combination of a therapeutically effective amount of a non-steroidal anti-inflammatory agent and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 25 235. The combination of Claim 234 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 30 236. The combination of Claim 234 or 235 wherein the nonsteroidal anti-inflammatory comprises indomethacin, naproxen and a combination thereof.
- 237. The combination of Claim 234 or 235 wherein the non-35 steroidal anti-inflammatory comprises [±] tromethamine salt of Ketorolac.
 - 238. For use to treat a patient suffering from HIV

(AIDS), the combination of a therapeutically effective amount of Ascorbic Acid (Vitamin C), a therapeutically effective amount of a non-steroidal anti-inflammatory and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

10

239. The combination of Claim 238 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

15

- 240. The combination of Claim 237 or 239 wherein the non-steroidal anti-inflammatory is indomethacin.
- 241. The combination of Claim 238, 239 or 240 further 20 comprising interferon.
- 242. The combination of Claim 238, 239, 240 or 241 further comprising Dimethyl Sulfoxide (DMSO) and wherein some or all of the forms of the hyaluronic acid may be substituted by therapeutically effective amount of dimethyl sulfoxide.
 - 243. For the use of Claim 174, 175 or 176 further comprising interferon.
- 30 244. For the use the Claim 174, 175, 176 or 243 further comprising dimethyl sulfoxide and wherein some or all of the forms of the hyaluronic acid may be substituted by therapeutically effective amounts of dimethyl sulfoxide.
- 35 245. For enhanced neoplastic activity and effect, the administration of a therapeutically effective amount of ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives,

complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 246. The use of Claim 245 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 247. For enhanced neoplastic activity and effect, the combination of a therapeutically effective amount of ascorbic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

20

5

10

248. The combination of Claim 247 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

25

35

- A method of increasing activity of macrophages in mammals suffering from disease, the administration of an effective amount of a non-steroidal anti-inflammatory agent (NSAID) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated sufficient to increase activity of macrophages in mammal suffering disease.
- 250. The use of Claim 249 wherein the hyaluronic acid and

PCT/CA90/00306

20

25

30

35

salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

- 5 251. The use of Claim 249 or 250 wherein the non-steroidal anti-inflammatory agent (NSAID) is selected from indomethacin, naproxen, and [±] tromethamine salt of Ketorolac.
- 10 252. For increasing activity of macrophages in mammals suffering from disease, the combination of an effective amount of a non-steroidal anti-inflammatory agent (NSAID) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters,
- fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated sufficient to increase activity of macrophages in mammal suffering disease.

253. The combination of Claim 252 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

254. The combination of Claim 252 or 253 wherein the non-steroidal anti-inflammatory agent (NSAID) is selected from indomethacin, naproxen, and $[\pm]$ tromethamine salt of Ketorolac.

255. A method of decreasing the side effects of administering a non-steroidal anti-inflammatory agent (NSAID) in a patient suffering a disease taking non-steroidal anti-inflammatory agent (NSAID), the administration of an effective amount of a non-steroidal anti-inflammatory agent (NSAID) for treating the patient and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of

hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated to decrease the side effects of the non-steroidal anti-inflammatory.

- 256. The use of Claim 255 wherein the non-steroidal antiinflammatory is indomethacin.
- 10 257. The use of Claim 255 wherein the non-steroidal antiinflammatory agent (NSAID) is selected from indomethacin, naproxen, and [±] tromethamine salt of Ketorolac.
- 258. For decreasing the side effects of administering a non-steroidal anti-inflammatory agent, the combination of an effective amount of a non-steroidal anti-inflammatory agent (NSAID) for treating the patient and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated to decrease the side effects of the non-steroidal anti-inflammatory.

25

- 259. The combination of Claim 258 wherein the non-steroidal anti-inflammatory is indomethacin.
- 260. The combination of Claim 258 wherein the non-30 steroidal anti-inflammatory agent (NSAID) is selected from indomethacin, naproxen, and [±] tromethamine salt of Ketorolac.
- 261. For the prevention of topical infection, the administration of an effective amount of an anti-metabolite and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the

agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.

- 5 262. For the use of Claim 261 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 10 263. For the prevention of topical infection, the combination of an effective amount of an anti-metabolite and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 264. The combination of Claim 263 wherein the hyaluronic 20 acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 25 265. For use to treat bone pain, muscle pain and/or inflammation, the administration of an effective amount of Ascorbic Acid (Vitamin C) and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 35 266. The use of Claim 265 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

- 267. For use to treat bone pain, muscle pain and/or inflammation, the combination of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 10 268. The combination of Claim 267 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 15 269. For enhancing prostaglandin synthesis inhibition, the combination of a therapeutically effective amount of aceytylsalicylic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 25 270. The combination of Claim 269 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.

271. For the use to enhance prostaglandin synthesis inhibition in a patient, the administration of a therapeutically effective amount of aceytylsalicylic acid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes

into the individual cells to be treated.

- 272. For the use of Claim 271 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.
- 273. For enhancing oxygenation of tissue by perfusion fluid bathing the tissue, the combination of perfusate fluid and a sufficient amount of hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, ésters, fragments and sub-units of hyaluronic acid to facilitate the agent at the site to be treated by the agents passing through the tissue (including scar tissue) through the cell membranes into the individual cells to be treated.
- 274. The combination of Claim 273 wherein the hyaluronic acid and salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and sub-units of hyaluronic acid is hyaluronic acid and/or salts thereof.